Immunogens of Pasteurella.

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The family Pasteurellaceae Pohl contains Gram-negative, facultatively anaerobic and fermentative bacteria of the genera Pasteurella, Haemophilus, and Actinobacillus. Approximately 20 different species of the genus Pasteurella have been identified using phenotypic and genetic analyses. Of these species, P. multocida and P. haemolytica are the most prominent pathogens in domestic animals causing severe diseases and major economic losses in the cattle, swine, sheep, and poultry industries. Mechanisms of immunity to these bacteria have been difficult to determine, and efficacious **vaccines** have been a challenge to develop and evaluate. **Pasteurella** multocida of serogroups A and D are mainly responsible for disease in North American poultry and pigs and to a lesser extent in cattle. Fowl cholera in chickens and turkeys is caused by various serotypes of P. multocida serogroup A and characterized by acute septicemia and fibrinous pneumonia or chronic fibrinopurulent inflammation of various tissues. Current biologicals in use are live P. multocida **vaccines** and bacterins. Potency tests for avian P. multocida biologicals are a bacterial colony count for **vaccines** and **vaccination** and challenge of birds for bacterins. Somatic antigens, particularly lipopolysaccharide (LPS), appear to be of major importance in immunity. In North American cattle, P. multocida serogroup A is associated mainly with bronchopneumonia (enzootic pneumonia) in young calves; however, it is occasionally isolated from fibrinous pleuropneumonia of feedlot cattle (shipping fever). Biologicals currently available are modified-live **vaccines** and bacterins. The potency test for **vaccines** is bacterial colony counts. The test for bacterin potency is **vaccination** and challenge of mice. Important immunogens have not been well characterized for P. multocida infection in cattle. In swine, P. multocida infection is sometimes associated with pneumonia; however, its major importance is in atrophic rhinitis. A protein toxin (dermonecrotic toxin), produced by toxigenic strains of P. multocida types A and D, and concurrent infection with Bordetella bronchiseptica appear to be the major factors in development of atrophic rhinitis. Currently available biologicals are bacterins and inactivated toxins (toxoids). The toxin appears to be the major immunogen for preventing atrophic rhinitis. There are, however, no standardized requirements for potency testing of P. multocida type D toxoid. Various serotypes of P. haemolytica biotype A are responsible for severe fibrinous pleuropneumonia of cattle and sheep, occasionally septicemia of lambs, and mastitis in ewes. Several serotypes of P. haemolytica biotype T are isolated from acute septicemia of lambs. The currently available P. haemolytica biologicals are modified-live **vaccines** , bacterins, bacterial surface extracts, and culture supernates that contain an exotoxin **leukotoxin**).(ABSTRACT TRUNCATED AT 400 WORDS)
(78 Refs.)

Efficacy of recombinant leukotoxin **in protection against pneumonic challenge with live** Pasteurella **haemolytica A1.**

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The recombinant **leukotoxin** (rLKT) of the bacterium **Pasteurella** haemolytica A1 was examined for its ability to protect cattle from experimental challenge with logarithmic-phase P. haemolytica. Six different **vaccines** were utilized in the experiment: P. haemolytica culture supernatant, P. haemolytica culture supernatant enriched with rLKT, rLKT alone, P. haemolytica culture supernatant enriched with Escherichia coli supernatant not containing LKT, E. coli supernatant alone, and phosphate-buffered saline. rLKT alone showed no protective capacity against development of clinical signs of respiratory disease or against development of postmortem lung lesions after experimental challenge. It was, however, shown to enhance the efficacy of the culture supernatant **vaccine** and decrease clinical signs and pneumonic lesions. The complexity of protective immunity in this disease is emphasized in this study, and, although LKT is an important virulence factor of the organism, an immune response to LKT alone does not protect animals against disease.

Tags: Animal; Support, Non-U.S. Gov't

Descriptors: Bacterial Toxins--Immunology--IM; *Bacterial **Vaccines** --Immunology--IM; *Exotoxins--Immunology--IM; * **Pasteurella** --Immunology --IM; *Pasteurellosis, Pneumonic--Prevention and Control--PC; Cattle; Recombinant Proteins--Immunology--IM

CAS Registry No.: 0 (leukotoxin); 0 (Bacterial Toxins); 0 (Bacterial Vaccines); 0 (Exotoxins); 0 (Recombinant Proteins)

Identification of RTX toxin target cell specificity domains by use of hybrid genes.

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The Escherichia coli hemolysin (HlyA) and **Pasteurella** haemolytica **leukotoxin** (LktA) are cytolytic toxins encoded by genes belonging to the recently described RTX gene family. These cytotoxins are, respectively, 1,023 and 953 amino acids in length and are encoded by genes within identically organized operons. They share 45% amino acid sequence identities but differ in their target cell specificities. In vitro-derived recombinant hybrid genes between hlyA and lktA were constructed by using restriction endonuclease sites created by oligonucleotide site-directed mutagenesis. The cytolytic activity of hybrid proteins was investigated using as targets sheep erythrocytes and two cultured cell lines from different species (BL3, bovine leukemia-derived B lymphocytes; and Raji, human B-cell lymphoma cells). HlyA is cytolytic to all three cell types. LktA lyses only BL3 cells. Among the hybrid proteins displaying cytolytic activity, the striking finding is that the hemolytic activity of several LktA-HlyA hybrids was independent of any cytolytic activity against either cultured cell species. The hemolytic activity was associated with the HlyA region between amino acids 564 and 739. Structures that are critical for HlyA cytolytic activity against BL3 or Raji cells were destroyed when LktA-HlyA and HlyA-LktA hybrids were made, respectively, at amino acid positions 564 and 739 of HlyA. In contrast to HlyA, which lysed the two different cultured cell lines with equal efficiency, Lkt-HlyA hybrids possessing the amino-terminal 169 residues of LktA lysed BL3 cells more efficiently than Raji cells. This suggests that a significant but not exclusive element of the LktA ruminant cell specificity resides in the amino-terminal one-fifth of the protein. A molecular model of the functional domains of HlyA and LktA is presented.

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